

Remarks

The present response is submitted in reply to the Office action issued on April 12, 2006. Claims 1-18 are pending in this application. Claims 6-17 are withdrawn from consideration and claims 1-5 and 18 are rejected. Claim 1 is canceled herewith. Claim 5 is amended in the present response. No new matter has been added. Reconsideration of the rejections is respectfully requested in light of the following remarks.

Rejection of Claims 1 & 5 under 35 U.S.C. 112, second paragraph and 35 U.S.C. 101

Claims 1 and 5 have been rejected under 35 U.S.C. 112, second paragraph. In particular, the Examiner states that the claims (1) provide for the use of the claimed invention, but do not set forth any steps involved in the method/process and (2) since it is unclear what method/process is intended to be encompassed. Claims 1 and 5 are also rejected under 35 U.S.C. 101 because the claimed recitation of a use without setting forth any steps in the involved process results in an improper definition of a process.

By way of the present response, claim 1 has been canceled. Therefore, this rejection is no longer germane with regard to claim 1. Claim 5 has been amended to delete the introductory phrase "Use or." As amended, claim 5 is a method claim which depends from claim 4 and is no longer indefinite. Withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-5 and 18 under 35 U.S.C. 103(a)

Claims 1-5 and 18 have been rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent Application No. 2005/0159377 (Ferguson, et al.), in view of U.S. Patent No. 4,278,674 (Egger, et al.). In particular, the Examiner states that the instant claims are

directed to a method of treating *Myobacterium* tuberculosis with pleuromutilins, specifically, 1-Tiamulin. Regarding the prior art; the Examiner argues that Ferguson, et al. teach that pleuromutilins possess antimicrobial activity and that pleuromutilins have activity over a wide range of bacteria, including *Myobacterium* tuberculosis. However, the Examiner notes that Ferguson, et al. fails to specifically teach 1-Tiamulin.

The Examiner then refers to Egger, et al., and argues that the secondary reference teaches a new class of pleuromutilins with antibacterial effects and that a preferred pleuromutilin is 14-desoxy-14-[(2-dimethylaminoethyl)mercaptoacetoxy]mutilin, otherwise known as 1-Tiamulin. The Examiner thus concludes that it would have been obvious to one having ordinary skill in the art to have substituted 1-Tiamulin as taught by Egger, et al. for the pleuromutilin as taught by Ferguson, et al., in order to arrive at the presently claimed invention.

The Examiner further argues that motivation for such combination would have been present since both Ferguson, et al. and Egger, et al. teach the use of pleuromutilin and both teach the art equivalency of pleuromutilins since both are disclosed to have antimicrobial properties. The Examiner finally concludes that there would thus be a reasonable expectancy of successfully treating *Myobacterium* tuberculosis with 1-Tiamulin. The applicant respectfully traverses this conclusion, as set forth below.

The applicant respectfully submits that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there

must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure (M.P.E.P. 2142; *In re Vacek*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Moreover, a conclusion of obviousness may not be based on impermissible hindsight (M.P.E.P. 2145(X)(A)), nor may the conclusion be based on an impermissible "obvious to try" rationale (M.P.E.P. 2145(X)(B)). An applicant may argue the examiner is applying an improper "obvious to try" rationale in support of an obviousness rejection. The admonition that "obvious to try" is not the standard under §103 has been directed mainly at two kinds of errors. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful (emphasis added).... In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it ((M.P.E.P. 2145(X)(B); *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)).

The Applicant respectfully submits that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at

the present invention. Additionally, any alleged motivation to do so would be based on impermissible hindsight and/or an improper obvious to try rationale. In light of the arguments set forth below, withdrawal of the present rejection is respectfully requested.

The Applicant respectfully submits that the present invention is patentably distinct from the aforementioned combination of teachings. Moreover, the Applicant submits that there would have been no motivation for one skilled in the art to have combined the teachings of Ferguson, et al. and Egger, et al. in order to arrive at the presently claimed invention.

The Applicant respectfully submits that Ferguson, et al. in paragraphs [0113] and [0114] provide for numerous – in fact at least forty-five – different genus types of microorganisms which pleuromutilins allegedly have activity over. In particular, these passages read as follows:

[0113] "Organism(s)" means a (i) prokaryote, including but not limited to, a member of the genus Streptococcus, Staphylococcus, Bordetella, Corynebacterium, Mycobacterium, Neisseria, Haemophilus, Actinomycetes, Streptomyces, Nocardia, Enterobacter, Yersinia, Fancisella, Pasturella, Moraxella, Acinetobacter, Erysipelothrix, Branhamella, Actinobacillus, Streptobacillus, Listeria, Calymmatobacterium, Brucella, Bacillus, Clostridium, Treponema, Escherichia, Salmonella, Kleibsiella, Vibrio, Proteus, Erwinia, Borrelia, Leptospira, Spirillum, Campylobacter, Shigella, Legionella, Pseudomonas, Aeromonas, Rickettsia, Chlamydia, Borrelia and Mycoplasma, and further including, but not limited to, a member of the species or group, Group A Streptococcus, Group B Streptococcus, Group C Streptococcus, Group D Streptococcus, Group G Streptococcus, Streptococcus pneumoniae,

Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus faecalis, Streptococcus faecium, Streptococcus durans, Neisseria gonorrhoeae, Neisseria meningitidis, Staphylococcus aureus, Staphylococcus epidermidis, Corynebacterium diphtheriae, Gardnerella vaginalis, Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium ulcerans, Mycobacterium leprae, Actinomyces israelii, Listeria monocytogenes, Bordetella pertussis, Bordetella parapertussis, Bordetella bronchiseptica, Escherichia coli, Shigella dysenteriae, Haemophilus influenzae, Haemophilus aegyptius, Haemophilus parainfluenzae, Haemophilus ducreyi, Bordetella, Salmonella typhi, Citrobacter freundii, Proteus mirabilis, Proteus vulgaris, Yersinia pestis, Klebsiella pneumoniae, Serratia marcescens, Serratia liquefaciens, Vibrio cholera, Shigella dysenteriae, Shigella flexneri, Pseudomonas aeruginosa, Francisella tularensis, Brucella abortus, Bacillus anthracis, Bacillus cereus, Clostridium perfringens, Clostridium tetani, Clostridium botulinum, Treponema pallidum, Rickettsia rickettsii and Chlamydia trachomatis, (ii) an archaeon, including but not limited to Archaeobacter, and (iii) a unicellular or filamentous eukaryote, including but not limited to, a protozoan, a fungus, a member of the genus Saccharomyces, Kluyveromyces, or Candida, and a member of the species Saccharomyces cerevisiae, Kluyveromyces lactis, or Candida albicans.

[0114] "Bacteria(um)" means a (i) prokaryote, including but not limited to, a member of the genus Streptococcus, Staphylococcus, Bordetella, Corynebacterium, Mycobacterium, Neisseria, Haemophilus, Actinomycetes, Streptomyces, Nocardia, Enterobacter, Yersinia, Francisella, Pasturella, Moraxella, Acinetobacter, Erysipelothrix, Branhamella, Actinobacillus, Streptobacillus, Listeria, Calymmatobacterium, Brucella, Bacillus, Clostridium, Treponema, Escherichia, Salmonella, Klebsiella, Vibrio, Proteus, Erwinia, Borrelia, Leptospira, Spirillum, Campylobacter, Shigella, Legionella, Pseudomonas, Aeromonas, Rickettsia, Chlamydia, Borrelia and Mycoplasma, and further including, but not limited to, a member of the species or group, Group A

Streptococcus, Group B Streptococcus, Group C Streptococcus, Group D Streptococcus, Group G Streptococcus, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus faecalis, Streptococcus faecium, Streptococcus durans, Neisseria gonorrhoeae, Neisseria meningitidis, Staphylococcus aureus, Staphylococcus epidermidis, Corynebacterium diphtheriae, Gardnerella vaginalis, Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium ulcerans, Mycobacterium leprae, Actinomyces israelii, Listeria monocytogenes, Bordetella pertussis, Bordetella parapertussis, Bordetella bronchiseptica, Escherichia coli, Shigella dysenteriae, Haemophilus influenzae, Haemophilus aegyptius, Haemophilus parainfluenzae, Haemophilus ducreyi, Bordetella, Salmonella typhi, Citrobacter freundii, Proteus mirabilis, Proteus vulgaris, Yersinia pestis, Klebsiella pneumoniae, Serratia marcescens, Serratia liquefaciens, Vibrio cholera, Shigella dysenteriae, Shigella flexneri, Pseudomonas aeruginosa, Francisella tularensis, Brucella abortus, Bacillus anthracis, Bacillus cereus, Clostridium perfringens, Clostridium tetani, Clostridium botulinum, Treponema pallidum, Rickettsia rickettsii and Chlamydia trachomatis, and (ii) an archaeon, including but not limited to Archaeobacter.

It is respectfully submitted that Ferguson, et al. simply recite a vast array of microorganisms in the section titled "Glossary" (between paragraphs [0091] and [0092]), but fail to specifically teach anywhere in the reference that pleuromutilins would have, or would be expected to have, activity over *Mycobacteria* in particular. To the contrary, it is respectfully submitted that one skilled in the art, when reviewing Ferguson, et al., would interpret the reference as relating primarily to the genus *Staphylococcus*, such as *Staphylococcus aureus* (paragraph [0120]) or *E. coli* (paragraph [0122]).

[0120] The invention discloses studies demonstrating that a range of pleuromutilins with various potencies in biochemical assays correlate with

antimicrobial, particularly that activity against bacteria, e.g., *Staphylococcus aureus*.

Moreover, paragraphs [0122] and [0125] refer to *E. coli* in addition to *Staphylococcus aureus* for use with the invention of Ferguson, et al., with no mention at all of *Mycobacteria*. Still further, claims 12 and 14 of Ferguson, et al. recite *Staphylococcus*, *Staphylococcus aureus*, *Staphylococcus* and *Staphylococcus pneumoniae*, with no recitation of *Mycobacteria*.

With regard to Egger, et al., the reference merely specifies antimicrobial activity of new pleuromutilins against *Staphylococcus aureus*, various *Streptococci* and various *Mycoplasmas* (col. 9, lines 1-9). However, no teaching or reference therein would lead one skilled in the art to associate the application of said new pleuromutilins of Egger, et al. to the *Mycobacteria* of the present invention.

It is therefore respectfully submitted that if one skilled in the art were to apply the new pleuromutilins of Egger, et al. for the pleuromutilins of Ferguson, et al., the skilled artisan would not necessarily arrive at the presently claimed invention of treating diseases mediated by *Mycobacterium*, comprising administering to a subject in need of such treatment an effective amount of a pleuromutilin. It is further respectfully submitted that there is simply no teaching, explicit or implicit, within Ferguson, et al. which would lead one skilled in the art to consider applying such a treatment to *Mycobacterium*. Ferguson, et al. provides no direction that pleuromutilins may specifically be used with *Mycobacterium* in the manner of the present invention; the only direction provided relates to *Staphylococcus aureus* or *E. coli*, as noted above. The Examiner is applying an

improper obvious to try rationale by trying each of the numerous possible choices until one possibly arrived at a successful result. There is no indication anywhere in Ferguson, et al. as to the direction as to which of these many possible choices would likely be successful, except as noted above. One skilled in the art would not, by merely applying the teaching of Egger, et al. to that of Ferguson, et al., instantly recognize the present invention of treating *Mycobacterium* by applying an effective amount of a pleuromutilin without trying each and every microorganism of the vast selection of microorganisms provided by Ferguson, et al. Moreover, it is respectfully submitted that the conclusion that one skilled in the art would arrive at such a conclusion would be based on impermissible hindsight. As noted above, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure. In the present instance, it is respectfully submitted that such teaching or suggestion to make the claimed combination and the reasonable expectation of success have been derived from the applicant's own disclosure and not from the cited prior art.

Therefore, in light of the aforementioned arguments, it is withdrawal of the present rejection is strongly requested.


Conclusion

In light of the foregoing claim amendments and arguments, it is believed that the present application is in condition for allowance, and such action is earnestly solicited.

The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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